# Chaining fragments in sequences: to sweep or not.

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**Abstract.** Computing an optimal chain of fragments is a classical problem in string algorithms, with important applications in computational biology. There exist two efficient dynamic programming algorithms solving this problem, based on different principles. In the present note, we show how it is possible to combine the principles of two of these algorithms in order to design a hybrid dynamic programming algorithm that combines the advantages of both algorithms.

#### 1 Introduction

The need for very efficient pairwise sequence alignments algorithm has motivated the development of methods aimed at breaking the natural quadratic time complexity barrier of dynamic programming alignment algorithms [5]. One of the successful alternative approaches is based on the technique of chaining fragments. Its principle is to first detect and score highly conserved factors, the *fragments* (also called *anchors* or *seeds*), then to compute a maximal score subset of fragments that are colinear and non-overlapping in both considered sequences, called an *optimal chain*. This optimal chain is then used as the backbone of an alignment, that is completed in a final stage by aligning the gaps located between consecutive selected fragments. This approach is used in several computational biology applications, such as whole genome comparison [13,1,7], cDNA/EST mapping [12], or identifying regions with conserved synteny.

In the present work we are interested in the problem of computing an optimal chain of fragments<sup>4</sup>, from a given set of k fragments, for two sequences t and u of respective lengths n and m. Due to its applications, especially in computational biology, this problem has received a lot attention from the algorithmic community [3,4,8,9,10,11,1]. The fragment chaining problem can be solved in  $O(k + n \times m)$  time by using a simple dynamic programming (DP) algorithm (see [9] for example). However, in practical applications, the number k of fragments can be subquadratic, which motivated the design of algorithms whose complexity depends only of k and can run in  $O(k \log k)$  worst-case time

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<sup>&</sup>lt;sup>4</sup> We focus here on the problem of computing the score of an optimal chain, but our algorithm can be complemented by a standard backtracking procedure to compute an actual optimal chain.

(see [8,4,10,12]). The later algorithms, known as Line Sweep (LS) algorithms, rely on geometric properties of the problem, where fragments can be seen as rectangles in the quarter plane, and geometric data structures that allow to retrieve and update efficiently (*i.e.* in logarithmic time) optimal subchains(see [12] for example).

This raises the natural question of deciding which algorithm to use to when comparing two sequences t and u. In particular, it can happen that the density of fragments differs depending on the location of the fragments in the considered sequences, due for example for the presence in repeats. In such cases, it might then be more efficient to rely on the DP algorithm in regions with high fragment density, while in regions of lower fragment density, the LS algorithm would be more efficient. This motivates the theoretical question we consider, that asks to design an efficient algorithm that relies on the classical DP principle when the density of fragments is high and switches to the LS principle when processing parts of the sequences with a low density of fragments. We show that this can be achieved, and we describe such a hybrid DP/LS algorithm for computing the score of an optimal chain of fragments between two sequences. We prove that our algorithm achieve a theoretical complexity that is as good as both the DP and LS algorithm, i.e. that for any instance, our algorithm performs as at least as well, in terms of theoretical worst-case asymptotic time complexity, as both the DP and the LS algorithm.

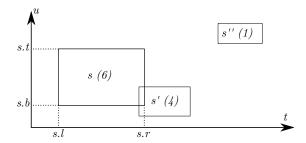
In Section 2, we introduce formally the fragment chaining problem and the DP and LS algorithms. In Section 3, we describe our hybrid algorithm and analyze its complexity.

## 2 Preliminaries

Preliminary definitions and problem statement. Let t and u be two sequences, of respective lengths n and m. We assume that positions index in sequences start at 0, so t[0] is the first symbol in t and t[n-1] its last symbol. As usual, by t[i,j] we denote the substring of t composed of symbols in positions  $i, i+1, \ldots, j$ .

A fragment is a factor that is common, possibly up to small variations, to t and u. Formally, a fragment s is defined by 5 elements  $(s.\ell, s.r, s.t, s.b, s.s)$ : the first four fields indicate that the corresponding substrings are  $t[s.\ell, s.r]$  and u[s.b, s.t], while the field s.s is a score associated to the fragment. We call borders of s the coordinates  $(s.\ell, s.b)$  and (s.r, s.t). As usual in chaining problems, we see fragments as rectangles in the quarter plane, where the x-axis corresponds to t and the y-axis to u. For a fragment s,  $s.\ell, s.r, s.b$  and s.t denote the left and right position of s over t and the bottom and top position of s over u ( $s.\ell \leq s.r$  and  $s.b \leq s.t$ ). See figure 1 for an example.

Let S denote a set of k fragments for t and u. A chain is a set of fragments  $\{s_1, \ldots, s_\ell\}$  such that  $s_i.r < s_{i+1}.\ell$  and  $s_i.t < s_{i+1}.b$  for  $i = 1, \ldots, \ell-1$ ; the score of a chain is the sum  $\sum_{i=1}^{\ell} s_i.s$  of the fragments it contains. A chain is optimal if there is no chain with a higher score. The problem we consider in the present work is to compute the score of an optimal chain.



**Fig. 1.** Example of the fragment chaining problem with three fragments represented by squares. Possible chains are [(s), (s'), (s''), (s, s''), (s', s'')]. The best chain is (s, s''), with a score of 7.

The dynamic programming (DP) algorithm. We first present a simple dynamic programming (DP) algorithm that computes an  $n \times m$  dynamic programming table M such that M[i][j] is the score of an optimal chain for the prefixes t[0,i] and u[0,j] (See pseudo-code 1). We present here a version that does not instantiate the full  $n \times m$  DP table, but records only the last filled column, following the classical technique introduced in [6] and used in the space-efficient fragment chaining DP algorithm described in [9].

The difference with Morgenstern's space efficient DP algorithm [9] is that we still require a quadratic space for the data structure L. In terms of computing the score of an optimal chain, the key point is that S[s], if defined, contains the optimal score of a chain that contains s as last fragment. The worst-case time complexity of this algorithm is obviously  $O(k + n \times m)$ .

The Line Sweep (LS) algorithm. We now describe a Line Sweep algorithm for the fragment chaining problem (See pseudo-code 2). The main idea is to process fragments according to their order in the sequence t, while maintaining a data structure that records, for each position i in u, the best partial chain found so far using only fragments below position i.

In this algorithm P stores all fragments borders, S[s], as in the DP algorithm, is the score of an optimal chain among all the chains that end with fragment s. A fragment s is said to have been processed after the entry (s.r, end, s.s) has been processed through the loop in line 8. A  $partial\ chain$  is a chain composed only of processed fragments.

The data structure A satisfies the following invariant, that is key to ensure the correctness of the algorithm: if (pos, type, s) is the last entry of P that has been processed, then A contains an entry (p, v) if and only if the best chaining score, among partial chains that belong to the rectangle defined by points (0, 0) and (pos, p), is v and corresponds to a chain ending with a fragment s' such that s'.t = p.

Line 16 ensures this invariant is maintained. This invariant allows to retrieve from A the score of an optimal partial chain that can be extended by the current

## Algorithm 1 The Dynamic Programming algorithm

```
1 L: an array of n \times m linked lists
2 S: an array of k integers
 3 M: an array of m integers
 4 foreach s in S do
 5
      front insert (s, end) into L[s.r][s.t]
6
      front insert (s, begin) into L[s.\ell][s.b]
 7 for i from 0 to n
 8
      left = 0
      leftDown = 0
9
10
      for j from 0 to m
         maxC = 0
11
12
         foreach (s, type) in L[i][j]
13
            if type is begin
14
               S[s] = s.s + leftDown
            if type is end and S[s] > maxC
15
               maxC = S[s]
16
17
         leftDown = left
18
         left = M[j]
19
         M[j] = max(M[j], M[j-1], maxC)
20 return M[m-1]
```

#### Algorithm 2 The Line Sweep algorithm

```
1 P: an array of 2k triples (position, type, fragment)
 2 A: a set of pairs (position, score)
 3 S: an array of k integers
 4 foreach s in S do
      insert (s.\ell, begin, s) into P
 6
      insert (s.r, end, s) into P
 7 sort P according to the field position, with begin positions appearing before end
        positions having the same value
 8 foreach (pos, type, s) in P
 9
       if type is begin
            retrieve from A the pair (p, v) such that p is the highest position strictly
10
                 less than s.b
            S[s] = s.s + v
11
       if type is end
12
            (p, v) = retrieve from A the highest position less or equal to s.t
13
14
            if S[s] > v
               retrieve from A the pair (p', v') such that v' is the highest score less
15
                    than or equal to S[s]
               remove from A all entries (p'', v'') such that p < p'' \le p'
16
17
               insert (s.t, S[s]) into A
18 (p, v) = last entry of A
19 return v
```

fragment s, *i.e.* that ends up in u in a position strictly smaller than s.b (line 11). This property follows from the fact that the order in which fragments are processed ensures that all previously processed fragments do not overlap with the current fragment in t.

In order to implement this algorithm efficiently, it is fundamental to ensure that in line 16, the time required to remove c entries (the set of all entries of A with first field strictly greater than p and lower than or equal to p') is  $O(c \log(k))$ . If A is implemented in a data structure that satisfies this property and support searches, insertions and deletions in logarithmic time, then the time complexity of the algorithm is  $O(k \log(k))$ ; see [12] for a discussion on such data structures.

## 3 An hybrid algorithm

We now describe an algorithm that combines both approaches described in the previous section.

Overview. We first introduce the notion of compact instance. An instance of the chaining problem is said to be compact, if each position of t and each position of t contains at least one border. If an instance is not compact, then there exists a unique compact instance obtained by removing from t and from t all positions that do not contain a fragment border, leading to sequences t' and t', and updating the fragments borders according to the sequences t' and t', leading to a set t' of fragments. From now, we denote by t', t', t' the compact instance corresponding to t', t', t', and t' and t' the lengths of t' and t'.

Next, we define, for a position p of t its border density  $\mathcal{K}_p$  as the number of fragment borders (i.e. number of fragments extremities) located in t[p]. If  $P^1$  is the set of positions in t' with border density strictly greater than  $\frac{m'}{\log m'-1}$ , and  $P^2$  the remaining  $n'-|P^1|$  positions of t', then the hybrid DP/LS algorithm we describe below has time complexity

$$O\left(k + \min(k\log(k), m) + \min(k\log(k), n) + \sum_{p \in P^1} (m' + \mathcal{K}_p) + \log(m') \sum_{p \in P^2} \mathcal{K}_p\right).$$

Intuitively, our hybrid algorithm works on a compact instance, and fills in the DP table for this compact instance, deciding for each column of this table (i.e. position of t') to fill it in using the DP equations or the Line Sweep principle, based on its border density.

Compacting an instance. We first describe how to compute the compact instance (t', u', S').

**Lemma 1.** The compact instance (t', u', S') can be computed in time  $O(k + \min(k \log(k), m) + \min(k \log(k), n))$  and space O(k + n + m).

The proof of this lemma is quite straightforward, and we omit the details here for space reason. Assume we are dealing with t (the same method applies to u).

- If  $k \log(k) \leq m$ , then we (1) sort the fragments extremities in t in increasing order of their starting position, (2) cluster together fragment extremities with the same value, and (3) relabel the coordinates of each fragment extremity using the number of clusters preceding it in the order, plus one.
- If  $k \log k > m$ , then we (1) detect positions of t with no fragment extremities, in O(k+m) time, (2) mark them and relabel the positions with non-zero density in O(m) time, and finally (3) relabel the fragment extremities according to the new labels of their positions, in O(k) time.

From now, we assume that the compact instance has been computed and that it is the considered instance.

DP update vs LS update. In this section, we introduce our main idea. The principle is to consider fragments in the same order than in the LS algorithm -i.e. through a loop through indices 0 to n'-1, a feature which is common to both the DP and LS algorithms -, but to process the fragments whose border in t' is in position i using either the DP approach if the density of fragments at t'[i] is high, or the LS approach otherwise. Hence, the key requirement will be that,

- when using the DP approach, the previous column of the DP table is available,
- when using the LS approach, a data structure with similar properties than data structure A used in the LS algorithm is available.

A hybrid data structure. We introduce now a data structure B that ensures that the above requirements are satisfied. The data structure B is essentially an array of m' entries augmented with a balanced binary search tree. Formally:

- We consider an array  $\mathcal{B}$  of m' entries, such that  $\mathcal{B}[i]$  contains chaining scores, and satisfies the following invariant: if s is the last processed fragment, for every  $i = 1, \ldots, s.r$ ,  $\mathcal{B}[i] \geq \mathcal{B}[i-1]$ .
- We augment this array with a balanced binary search tree  $\mathcal{C}$  whose leaves are the entries of  $\mathcal{B}$  and whose internal nodes are labeled in order to satisfy the following invariant: a node x is labeled by the maximum of the labels of its right child and left child.

The data structure B will be used in a similar way than the data structure A of the LS algorithm, *i.e.* to answer the following queries: given  $0 \le p \le m'$ , find the optimal score of a partial chain whose last fragment s satisfies  $s.t \le p$ . This principle is very similar to solutions recently proposed for handling dynamic minimum range query requests [2].

We describe now how we implement this data structure using an array. Let b be the smallest integer such that  $m' \leq 2^b$ . We encode B into an array of size  $2^{b+1}$ , whose prefix of length m'-1 contains the labels of the internal nodes of

the binary tree  $\mathcal{C}$  (so each cell contains a label and the indexes to two other cells, corresponding respectively to the left child and right child), ordered in breadth-first order, while the entries of  $\mathcal{B}$  are stored in the suffix of length m' of the array (see figure 2). From now, we identify nodes of the binary tree and cells of the array, that we denote by B.

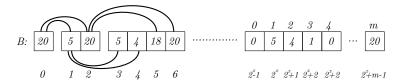


Fig. 2. Example of the implementation of the data structure B with an array.

Using this implementation, for a given node of the binary search tree, say encoded by the cell in position x in B (called node x from now), we can quickly obtain the position, in the array, of its left child, of its right child, but also of its parent (if B[x] is not the root) and of its rightmost descendant, defined as the unique node reached by a maximal path of edges to right children, starting at x edges to a left (resp. right) child. Indeed, it is straightforward to verify that, the constraint of ordering the nodes of the binary tree in the array according to a breadth-first order implies that, for node x, if y is the largest integer such that  $2^y \le x + 1$  and  $z = x - 2^y + 1$ , then:

```
\begin{array}{l} - \text{ if } x \geq 2^b - 1, \ x \text{ is a leaf;} \\ - \ leftChild(x) = 2^{y+1} - 1 + 2*z \text{ if } x \text{ is not a leaf;} \\ - \ rightChild(x) = 2^{y+1} - 1 + 2*z + 1 \text{ if } x \text{ is not a leaf;} \\ - \ parent(x) = -1 \text{ if } x = 0 \ (x \text{ is the root);} \\ - \ parent(x) = 2^{y-1} - 1 + \left|\frac{z}{2}\right| \text{ if } x \neq 0; \\ - \ rightmostChild(x) = 2^b - 1 + (z+1)2^{b-z} - 1. \end{array}
```

Implementing the DP and LS algorithms with the hybrid data structure. It is then easy to implement the DP algorithm using the data structure B, by using  $\mathcal{B}$  as the current column of the DP table (i.e. if the currently processed position of t' is i,  $\mathcal{B}[j]$  is the score of the best partial chain included in the rectangle defined by (0,0) and (i,j), without updating the internal nodes of the binary search tree  $\mathcal{C}$ .

To implement the LS algorithm, the key points are

- to be able to update efficiently the data structure B, when a fragment s has been processed;
- to be able to find the best score of a partial chain ending up at a position in u' strictly below p.

## **Algorithm 3** Set a chaining score for a position p.

```
\begin{array}{ll} 1 \ setScore(B,p,score): \\ 2 & index = 2^b - 1 + p \ / / \ start \ from \ leaf \ corresponding \ to \ p \\ 3 & \mathbf{while} \ index! = -1 \ \&\& \ B[index] < score \\ 4 & B[index] = score \\ 5 & index = parent(index) \end{array}
```

## **Algorithm 4** Retrieve the best chaining score for partial chains ending strictly below position p.

```
1 \ getBestScore(B, p):
2
      let b be the smallest integer s.t. m' \leq 2^b
3
      maxScore=0
      currentNode = 0 // the \ root \ node
4
      indexOfP = 2^b - 1 + p
5
6
      \mathbf{while}\ rightmostChild(currentNode) > indexOfP
7
         left = leftChild(currentNode)
         if \ rightmostChild(left) >= indexOfP \ // \ move \ left
8
9
            ncurrentNode = left
10
         else // move right
            maxScore = max(maxScore, B[left])
11
12
            currentNode = rightChild(currentNode) \\
13
      return max(maxScore, B[currentNode])
```

Updating B can be done through the function setScore below, with parameters p = s.t and score = S[s], while the second task can be achieved by the function getBestScore described below, which is a simple binary tree search.

It is straightforward to see that if all updates of B are done using the function setScore, then the two required invariants on B are satisfied. The time complexity of both setScore and getBestScore is in  $O(\log(m'))$ , due to the fact that the binary tree is balanced. So now, we can implement the LS algorithm on compact instances using the data structure B by replacing the instruction in line 11 of the LS algorithm by a call to getBestScore(B, s.b), the block of instructions in lines 13-17 by setScore(B, S[s]) and reading the optimal chain score in the root of the binary tree. The complexity of operations over B are logarithmic in m' that is less or equal to k. Thus the overall time complexity is in  $O(k \log m')$ .

LS/DP update with the hybrid data structure. So, in an hybrid algorithm that relies on the data structure B, when the algorithm switches approaches (from DP to LS, or LS to DP), the data structure B is assumed to be consistent for the current approach, and needs to be updated to become consistent for the next approach.

So when switching from DP (say position i-1,  $i=1,\ldots n'$ ) to LS (position i), we assume that  $\mathcal{B}[j]$  ( $j=0,\ldots,m'-1$ ) is the optimal score of a partial chain in the rectangle defined by (0,0) and (i-1,j), and we want to update B in such a way that the label of any internal node x of the binary tree is the maximum of both its children. As  $\mathcal{B}$  are the leaves of the binary tree, this update can be done during a post-order traversal of the binary tree, so in time O(m').

When switching from LS to DP (say to use the DP approach on position i while the LS approach was used on position i-1), we assume that for every leaf  $\mathcal{B}[j]$  of the binary tree corresponding to a position at most i-1, the value in  $\mathcal{B}[j]$  is the optimal score of a partial chain in the whose last fragment ends in position i-1; this follows immediately from the way labels of the leaves of the binary tree are inserted by the setScore function. To update B, we want that in fact  $\mathcal{B}[j]$  is the optimal score of a partial chain in the whose last fragment ends in position at most i-1. So the update function needs only to give to  $\mathcal{B}[j]$  the value  $\max_{0 \le j' \le j} \mathcal{B}[j']$ , which can again be done in time O(m').

So updating the data structure B from DP to LS or LS to DP can be done in time O(m'). We denote by *update* the function performing this update.

Deciding between LS and DP using the fragment density. Before we can finally introduce our algorithm, we need to address the key point of how to decide which paradigm (DP or LS) to use when processing the fragments having a border in the current position of t, say c. Let  $\mathcal{K}_c$  be the number of fragments s such that  $s.\ell = c$  or s.r = c. Using the DP approach, the cost of updating  $\mathcal{B}$  (i.e. to compute the column c of the DP table) is  $O(m' + \mathcal{K}_c)$ . With the LS approach, the cost of updating B is in  $O(\mathcal{K}_c \log m')$ .

So, if  $\mathcal{K}_c > \frac{m'}{\log m' - 1}$ , the asymptotic cost of the DP approach is better than the asymptotic cost of the LS approach, while it is the converse if  $\mathcal{K}_c \leq \frac{m'}{\log m' - 1}$ .

So, prior to processing fragments, for each position i in t (i = 0, ..., m' - 1), we record in an array C is fragments borders in position i are processed using the DP approach (C[i] contains DP) or the LS approach (C[i] contains LS). This last observation leads to our main result, Algorithm 5 below.

### Algorithm 5 A hybrid algorithm for the fragment chaining problem.

```
1 compute the compact instance (t', u', \mathcal{S}')
 2 L1: an array of n' \times 2 linked lists
 3 C: an binary array of size n'
 4 foreach s in S' do
      if C[s.r] is DP then front insert (s, end, s.t) into L1[s.r][1]
 5
       else front insert (s, end) into L1[s.r][0]
 6
 7
      if C[s.\ell] is DP then front insert (s, begin, s.b) into L1[s.\ell][1]
       else front insert (s, begin) into L1[s.\ell][0]
 9 B: a binary tree for m' leafs (all nodes are set to zero)
10 \mathcal{B}: refers to the m' leaves of B
11 S: an array of integer of size k
12 for i from 0 to n' do
13
       if C[i] \neq C[i-1] then update(B)
14
       if C[i] is DP
          L2: an array of m' linked lists
15
16
          for each (s, t, j) in L1[i][1] do front insert (s, t) into L2[j]
          left = 0, leftDown = 0
17
          for j from 0 to m' do
18
             maxC = 0
19
20
             foreach (s, type) in L2[j] do
                 if type is begin then S[s] = s.s + leftDown
21
                 if type is end and S[s] > maxC then maxC = S[s]
23
             leftDown = left, left = \mathcal{B}[j]
24
             \mathcal{B}[j] = max(\mathcal{B}[j], \mathcal{B}[j-1], maxC)
       else //C[i] is LS
25
26
          foreach (s, type) in L1[i][0] do
27
              if type is begin then S[s] = s.s + getBestScore(B, s.b)
              if type is end then setScore(B, s.t, S[s])
29 if C[n'-1] is direct then return \mathcal{B}[m'-1]
30 else return value of the root of B
```

Time and space complexity. In terms of space complexity, the algorithm, we avoid to use  $O(k+n'\times m')$  space for storing the fragments borders in  $n'\times m'$  lists (structure L of the DP algorithm) by using two lists: L1[i] stores all fragments borders in position i of t', while L2[j] stores all fragments borders in position i of t' and j of u', and is computed from L[1]. So the total space requirement is in O(k+m'+n').

We now establish the time complexity of this algorithm. If the current position i of t is tagged as DP, the cost for updating the column is  $O(m' + \mathcal{K}_i)$ , including the cost of setting up L2 from L1, that is proportional to the number of fragments borders in the current position (line 14–24). If C[i] is LS, the cost for computing chains scores on this position is  $O(\mathcal{K}_i \log m')$  (line 25–28). Thus, if we call  $P^1$  the set of positions on t where we use the DP approach,  $P^2$  the set of positions on t where we use the LS approach and  $P = P^1 \cup P^2$ , the time for the whole loop at line 12 is

$$O\left(\sum_{p\in P^1} (m' + \mathcal{K}_p) + \sum_{p\in P^2} \mathcal{K}_p \log m'\right)$$

We have  $|P^1| + |P^2| = n'$ ,  $\forall p \in P^1 : \mathcal{K}_p > \frac{m'}{\log m' - 1}$  and  $\forall p \in P^2 : \mathcal{K}_p \leq \frac{m'}{\log m' - 1}$ . Moreover, updating the data structure B from LS to DP or DP to LS (line 13) is done at most one more time then the size of  $P^1$ , so the total cost of this operation is  $O\left(\sum_{p \in P^1} m'\right)$ , and can thus be integrated, asymptotically, to the cost of processing the positions in  $P^1$ .

Theorem 1. The hybrid algorithm computes an optimal chain score in time

$$O\left(k + \min(k \log k, m) + \min(k \log k, n) + \sum_{p \in P^1} (m' + \mathcal{K}_p) + \log m' \sum_{p \in P^2} \mathcal{K}_p\right)$$
(1)

and space O(k+n+m).

To conclude the complexity analysis, we show that the hybrid algorithm performs at least as well, asymptotically, than both the DP and the LS algorithms. From (1), we deduce that, if  $P^2 = P$ , the hybrid algorithm time complexity becomes  $O(k + \min(k \log k, m) + \min(k \log k, n) + \log m'k)$ , which is at worst equal to the asymptotic worst-case time complexity of the LS algorithm as  $m' = \min(m, k)$ .

Now, if  $P^2 \neq P$ , for every position c in  $P^1$ , we know that the cost of updating B and processing c with the DP approach is not worse than processing it with the LS approach, by the value chosen for  $\mathcal{K}_c$ . This ensures that, asymptotically, the hybrid algorithm does perform at least as well as the LS algorithm.

We consider now the DP algorithm. Again, from (1), if  $P^1 = P$ , the complexity becomes  $O(k + \min(k \log k, m) + \min(k \log k, n) + m'n')$ , which is equal to the original dynamic programming algorithm time complexity as  $n' = \min(n, k)$  and  $m' = \min(m, k)$ .

As above, if we assume now that  $P^1 \neq P$ , then we know that the cost of processing the positions of  $P^2$  with the LS approach is asymptotically not worse than processing them with the DP algorithm. The cost of updating B from switching from DP to LS can be integrated into the asymptotic cost of the DP part. This shows that the hybrid algorithm is, asymptotically, not worse than the pure DP algorithm.

#### 4 Discussion

Our main result in the present paper is an hybrid algorithm that combines the positive features of both the classical dynamic programming and of the line sweep algorithm for the fragment chaining problem. We did show that a simple data structure can be used to alternate between both algorithmic principles, thus benefiting of the positive behavior of both algorithms. Not surprisingly, the choice between using the DP or the LS principle is based on fragments density.

It is easy to define instances where the hybrid algorithm performs better asymptotically, than both the DP and LS algorithms. For example, if  $m=n^{\frac{4}{5}}$ and  $k=2n^{\frac{3}{2}}$  and there are  $n^{\frac{3}{2}}$  seeds extremities on t[0] and  $n^{\frac{3}{2}}$  extremities on t[n-1], all other extremities spread along t and u, we can show that the complexities are  $O(n^{\frac{9}{5}})$  for the DP algorithm,  $O(n^{\frac{3}{2}} \log n)$  for the LS algorithm and  $O(n^{\frac{3}{2}})$  for the hybrid algorithm. However, so far our result is mostly theoretical. The threshold of  $m'/(\log(m')-1)$  considered on real genome data is high, as it assumes a very high vfragment density that is unlikely to be observed often, at least on applications such the alignment of whole bacterial genomes for example. Preliminary experiments on such dfatya following t5he approach developped in [13] show that the LS algorithm is slightly more efficient than the hybrid one. So it remains to be seen if it could result in an effective speed-up when chaining fragments in actual biological applications, especially involving high-throughput sequencing data or overlapping fragments [13]. From a practical point of view, it is also of interest to consider algorithm engineering appects, especially related to the hybrid data structure, to see if this could alleviate the issue of the high density threshold required to switch between the LS and DP approaches, and assess the practical interest of the novel theoretical framework we introduced in the present paper.

#### References

- 1. M.I. Abouelhoda and E. Ohlebusch. Chaining algorithms for multiple genome comparison. *J. Discrete Algorithms* 3, pp. 321–341, 2005.
- L. Arge, J. Fischer, P. Sanders, and N. Sitchinava. On (Dynamic) Range Minimum Queries in External Memory. In WADS 2013, vol. 8037 of LNCS, pp. 37–48. 2013.
- 3. D. Eppstein, Z. Galil, R. Giancarlo, and G. F. Italiano. Sparse dynamic programming. I: linear cost functions; II: convex and concave cost functions, *J. Assoc. Comput. Mach.* 39, pp. 519–567, 1992.
- 4. S. Felsner, R. Müller and L. Wernisch. Trapezoid graphs and generalizations, geometry and algorithms. *Discrete Appl. Math.* 74, pp. 13–32, 1997.
- D. Gusfield. Algorithms on Strings, Trees and Sequences. Cambridge University Press, 1997.
- 6. D.S. Hirschberg. A linear space algorithm for computing maximal common subsequences. *Comm. Assoc. Comput. Mach.* 18, pp. 341–343, 1975.
- 7. M. Höhl, S. Kurtz and E. Ohlebusch. Efficient multiple genome alignment. *Bioinformatics* 18, pp. S312–S320, 2002.

- 8. D. Joseph, J. Meidanis, and P. Tiwari. Determining DNA sequence similarity using maximum independent set algorithms for interval graphs. In *SWAT 1992*, vol. 621 of *LNCS*, pp. 326–337. 1992.
- 9. B. Morgenstern. A simple and space-efficient fragment-chaining algorithm for alignment of DNA and protein sequences. *Appl. Math. Lett.* 15, pp. 11–16, 2002,
- 10. G. Myers and W. Miller. Chaining multiple-alignment fragments in sub-quadratic time. In  $SODA\ 1995$ , pp. 38–47, 1995.
- 11. G. Myers, and X. Huang. An  $O(N^2 \log N)$  restriction map comparison and search algorithm. Bull. Math. Biol., 54, pp. 599–618, 1992.
- E. Ohlebusch and M.I. Abouelhoda. Chaining Algorithms and Applications in Comparative Genomics. In (S. Aluru, ed.) Handbook of Computational Molecular Biology. CRC Press, 2005.
- R. Uricaru, A. Mancheron and E. Rivals. Novel Definition and Algorithm for Chaining Fragments with Proportional Overlaps. J. Comput. Biol. 18, pp. 1141– 1154, 2011.